



568.1D1.TXT

SEQUENCE LISTING

<110> Madison, Edwin L

<120> TISSUE TYPE PLASMINOGEN ACTIVATOR (t-PA)
VARIANTS: COMPOSITIONS AND METHODS OF USE

<130> TSRI 568.1D1

<140> US 10/705,633
<141> 2003-11-10

<150> US 09/600,985
<151> 2000-11-13

<150> PCT/US97/20226
<151> 1997-11-12

<150> US 60/030,655
<151> 1996-11-12

<160> 10

<170> FastSEQ for Windows Version 4.0

<210> 1
<211> 527
<212> PRT
<213> Homo sapiens

<400> 1
Ser Tyr Gln Val Ile Cys Arg Asp Glu Lys Thr Gln Met Ile Tyr Gln
1 5 10 15
Gln His Gln Ser Trp Leu Arg Pro Val Leu Arg Ser Asn Arg Val Glu
20 25 30
Tyr Cys Trp Cys Asn Ser Gly Arg Ala Gln Cys His Ser Val Pro Val
35 40 45
Lys Ser Cys Ser Glu Pro Arg Cys Phe Asn Gly Gly Thr Cys Gln Gln
50 55 60
Ala Leu Tyr Phe Ser Asp Phe Val Cys Gln Cys Pro Glu Gly Phe Ala
65 70 75 80
Gly Lys Cys Cys Glu Ile Asp Thr Arg Ala Thr Cys Tyr Glu Asp Gln
85 90 95
Gly Ile Ser Tyr Arg Gly Thr Trp Ser Thr Ala Glu Ser Gly Ala Glu
100 105 110
Cys Thr Asn Trp Asn Ser Ser Ala Leu Ala Gln Lys Pro Tyr Ser Gly
115 120 125
Arg Arg Pro Asp Ala Ile Arg Leu Gly Leu Gly Asn His Asn Tyr Cys
130 135 140
Arg Asn Pro Asp Arg Asp Ser Lys Pro Trp Cys Tyr Val Phe Lys Ala
145 150 155 160
Gly Lys Tyr Ser Ser Glu Phe Cys Ser Thr Pro Ala Cys Ser Glu Gly
165 170 175
Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr Arg Gly Thr His
180 185 190
Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn Ser Met Ile
195 200 205

568.1D1.TXT

Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala Gln Ala Leu
 210 215 220
 Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly Asp Ala Lys
 225 230 235 240
 Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp Glu Tyr Cys
 245 250 255
 Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro
 260 265 270
 Gln Phe Glu Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro
 275 280 285
 Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg
 290 295 300
 Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala
 305 310 315 320
 Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile
 325 330 335
 Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Glu Gln Lys Phe
 340 345 350
 Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr
 355 360 365
 Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys
 370 375 380
 Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu Pro Pro Ala Asp
 385 390 395 400
 Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly Tyr Gly Lys
 405 410 415
 Asp Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Lys Glu Ala His
 420 425 430
 Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn
 435 440 445
 Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly
 450 455 460
 Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly
 465 470 475 480
 Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile
 485 490 495
 Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val Pro Gly Val Tyr Thr
 500 505 510
 Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp Asn Met Arg Pro
 515 520 525

<210> 2
 <211> 527
 <212> PRT
 <213> Homo sapiens

<400> 2
 Ser Tyr Gln Val Ile Cys Arg Asp Glu Lys Thr Gln Met Ile Tyr Gln
 1 5 10 15
 Gln His Gln Ser Trp Leu Arg Pro Val Leu Arg Ser Asn Arg Val Glu
 20 25 30
 Tyr Cys Trp Cys Asn Ser Gly Arg Ala Gln Cys His Ser Val Pro Val
 35 40 45
 Lys Ser Cys Ser Glu Pro Arg Cys Phe Asn Gly Gly Thr Cys Gln Gln
 50 55 60
 Ala Leu Tyr Phe Ser Asp Phe Val Cys Gln Cys Pro Glu Gly Phe Ala
 65 70 75 80
 Gly Lys Cys Cys Glu Ile Asp Thr Arg Ala Thr Cys Tyr Glu Asp Gln

568.1D1.TXT

	85	90	95
Gly Ile Ser Tyr Arg Gly Thr Trp Ser	100	105	110
Thr Ala Glu Ser Gly Ala Glu			
Cys Thr Asn Trp Asn Ser Ser Ala Leu Ala Gln Lys Pro Tyr Ser Gly	115	120	125
Arg Arg Pro Asp Ala Ile Arg Leu Gly Leu Gly Asn His Asn Tyr Cys	130	135	140
Arg Asn Pro Asp Arg Asp Ser Lys Pro Trp Cys Tyr Val Phe Lys Ala	145	150	155
Gly Lys Tyr Ser Ser Glu Phe Cys Ser Thr Pro Ala Cys Ser Glu Gly	165	170	175
Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr Arg Gly Thr His	180	185	190
Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn Ser Met Ile	195	200	205
Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala Gln Ala Leu	210	215	220
Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly Asp Ala Lys	225	230	235
Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp Glu Tyr Cys	245	250	255
Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro	260	265	270
Gln Phe Glu Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro	275	280	285
Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg	290	295	300
Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala	305	310	315
Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile	325	330	335
Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Gln Lys Phe	340	345	350
Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr	355	360	365
Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys	370	375	380
Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu Pro Pro Ala Asp	385	390	395
Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly Tyr Gly Lys	405	410	415
Glu Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Lys Glu Ala His	420	425	430
Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn	435	440	445
Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly	450	455	460
Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly	465	470	475
Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile	485	490	495
Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val Pro Gly Val Tyr Thr	500	505	510
Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp Asn Met Arg Pro	515	520	525

<210> 3
<211> 527

<212> PRT
<213> Homo sapiens

<400> 3
Ser Tyr Gln Val Ile Cys Arg Asp Glu Lys Thr Gln Met Ile Tyr Gln
1 5 10 15
Gln His Gln Ser Trp Leu Arg Pro Val Leu Arg Ser Asn Arg Val Glu
20 25 30
Tyr Cys Trp Cys Asn Ser Gly Arg Ala Gln Cys His Ser Val Pro Val
35 40 45
Lys Ser Cys Ser Glu Pro Arg Cys Phe Asn Gly Gly Thr Cys Gln Gln
50 55 60
Ala Leu Tyr Phe Ser Asp Phe Val Cys Gln Cys Pro Glu Gly Phe Ala
65 70 75 80
Gly Lys Cys Cys Glu Ile Asp Thr Arg Ala Thr Cys Tyr Glu Asp Gln
85 90 95
Gly Ile Ser Tyr Arg Gly Thr Trp Ser Thr Ala Glu Ser Gly Ala Glu
100 105 110
Cys Thr Asn Trp Asn Ser Ser Ala Leu Ala Gln Lys Pro Tyr Ser Gly
115 120 125
Arg Arg Pro Asp Ala Ile Arg Leu Gly Leu Gly Asn His Asn Tyr Cys
130 135 140
Arg Asn Pro Asp Arg Asp Ser Lys Pro Trp Cys Tyr Val Phe Lys Ala
145 150 155 160
Gly Lys Tyr Ser Ser Glu Phe Cys Ser Thr Pro Ala Cys Ser Glu Gly
165 170 175
Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr Arg Gly Thr His
180 185 190
Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn Ser Met Ile
195 200 205
Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala Gln Ala Leu
210 215 220
Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly Asp Ala Lys
225 230 235 240
Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp Glu Tyr Cys
245 250 255
Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro
260 265 270
Gln Phe Glu Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro
275 280 285
Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg
290 295 300
Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala
305 310 315 320
Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile
325 330 335
Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Gln Lys Phe
340 345 350
Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr
355 360 365
Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys
370 375 380
Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu Pro Pro Ala Asp
385 390 395 400
Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly Tyr Gly Lys
405 410 415
His Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Tyr Glu Ala His
420 425 430
Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn

568.1D1.TXT

435	440	445	
Arg Thr Val Thr Asp Asn Met	Leu Cys Ala Gly Asp Thr Arg Ser Gly		
450	455	460	
Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly			
465	470	475	480
Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile			
485	490	495	
Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val Pro Gly Val Tyr Thr			
500	505	510	
Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp Asn Met Arg Pro			
515	520	525	

<210> 4
<211> 290
<212> DNA
<213> Homo sapiens

<400> 4
ctacggcaag catgaggcct tgttccttt ctattcgag cggctgaagg aggctcatgt 60
cagactgtac ccatccagcc gtcacatc acaacatatta cttAACAGAA cagtcaccga 120
caacatgctg tgtgctggag acactcgag cggcggggcc caggcaaact tgcacgacgc 180
ctgccaggc gattcgggag gccccctgggt gtgtctgaac gatggccgca tgacttttgt 240
ggcatacatc agctggggcc tggctgtgg acagaaggat gtcccggtg 290

<210> 5
<211> 290
<212> DNA
<213> Homo sapiens

<400> 5
ctacggcaag gacgaggcct tgttccttt ctattcgag cggctgaagg aggctcatgt 60
cagactgtac ccatccagcc gtcacatc acaacatatta cttAACAGAA cagtcaccga 120
caacatgctg tgtgctggag acactcgag cggcggggcc caggcaaact tgcacgacgc 180
ctgccaggc gattcgggag gccccctgggt gtgtctgaac gatggccgca tgacttttgt 240
ggcatacatc agctggggcc tggctgtgg acagaaggat gtcccggtg 290

<210> 6
<211> 290
<212> DNA
<213> Homo sapiens

<400> 6
ctacggcaag gaggaggcct tgttccttt ctattcgag cggctgaagg aggctcatgt 60
cagactgtac ccatccagcc gtcacatc acaacatatta cttAACAGAA cagtcaccga 120
caacatgctg tgtgctggag acactcgag cggcggggcc caggcaaact tgcacgacgc 180
ctgccaggc gattcgggag gccccctgggt gtgtctgaac gatggccgca tgacttttgt 240
ggcatacatc agctggggcc tggctgtgg acagaaggat gtcccggtg 290

<210> 7
<211> 290
<212> DNA
<213> Homo sapiens

<400> 7
ctacggcaag catgaggcct tgttccttt ctattcgag cggctgtatg aggctcatgt 60
cagactgtac ccatccagcc gtcacatc acaacatatta cttAACAGAA cagtcaccga 120
caacatgctg tgtgctggag acactcgag cggcggggcc caggcaaact tgcacgacgc 180
ctgccaggc gattcgggag gccccctgggt gtgtctgaac gatggccgca tgacttttgt 240

568.1D1.TXT
gggcatcatc agctggggcc tgggctgtgg acagaaggat gtcccggtg 290
<210> 8
<211> 23
<212> DNA
<213> Homo sapiens

<400> 8
ctacggcaag gacgaggcct tgt 23

<210> 9
<211> 23
<212> DNA
<213> Homo sapiens

<400> 9
ctacggcaag gaggaggcct tgt 23

<210> 10
<211> 26
<212> DNA
<213> Homo sapiens

<400> 10
cggagcggct gtatgaggct mcatgt 26